9:15

## 780-4 Thrombin and Rheologic Factors – Clinical Relevance for the Development of Restenosis Following Elective PTCA in Patients With Stable Angina Pectoris

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Thrombosis secondary to severe vascular injury following PTCA is regarded to be a confounding factor in the pathogenesis of restenosis. The potential relevance of hemostatic risk factors has not been conclusively clarified so far.

In 46 consecutive patients, who underwent elective and primarily successful PTCA, fibrinogen (Fib), prothrombinfragment 1 + 2 (F1 + 2), plasma viscosity (PV), red cell aggregation (RBC) and endogenous fibrinolysis (tissue plasminogen activator antigen (t-PA), plasminogen activator inhibitor activity (PAI), plasmin 2 antiplasmin (PAP) were assesed prior to cardiac catheterization. Angiographic results were evaluated by quantitative coronary angiography.

Of these patients 14 (30%) suffered restenosis (stenosis >50%) and in comparison to patients without restenosis demonstrated elevations of fibrinogen (350 ± 57 vs. 305 ± 68 mg/dl, $p < 0.05$), PV (1.37 ± 0.07 vs. 1.32 ± 0.08 mPas, $p < 0.05$), RBC (14.0 ± 2.9 vs. 11.3 ± 2.8 U, $p < 0.01$) and F1 + 2 (1.4 ± 0.38 vs. 0.87 ± 0.38 nmol/l, $p < 0.05$). PAI (4.12 ± 1.86 vs. 5.15 ± 3.33 U/ml, n.s.), t-PA (9.00 ± 3.02 vs. 8.65 ± 2.8 ng/ml, n.s.) and PAP (458 ± 160 vs. 394 ± 128 g/l) as well as procedural variables of angioplasty did not differ significantly. Discriminative analysis revealed generation of thrombin (F1 + 2) to be the most important factor for the occurence of restenosis and late luminal loss correlated significantly with F1 + 2 ($r = 0.38$). In patients with F1 + 2 > 1.1 nmol/l and RBC > 12.3 U the rate of restenosis was 67%.

The results indicate that thrombin generation (F1 ± 2) and rheologic factors as assesed prior to mechanical injury have an influence on late restenosis following coronary angioplasty, which may contribute to a risk stratified use of antithrombotic therapy.

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## 780-5 Increased release of the soluble endothelial adhesion molecule ICAM-1 but not ELAM-1 during episodes of angina pectoris

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*Background:* Myocardial ischemia is known to result in activation of neutrophils, which subsequently adhere to endothelial cells via surface adhesion molecules expressed by both cell types. Leukocyte adhesion to the endothelium may result in coronary capillary plugging and impairment of coronary blood flow. Adhesion molecules such as ICAM-1 and E-selectin (ELAM-1) may be shed from the endothelial cell surface into the circulation and be detected in their soluble form.

*Aim:* The purpose of this study was to verify whether the myocardial ischemia occurring during angina episodes was associated with increased release of the soluble adhesion molecules ICAM-1 and ELAM-1.

*Methods:* Plasma samples were obtained during pain (DP) from 15 patients admitted to the emergency room with angina and 15 patients with non-cardiac chest pain (NCCP). To confirm diagnosis, patients underwent exercise stress test and, if not conclusive, $Tc^{99}$ MIBI SPECT or angiography. Convalescent sample was also taken from each patient in the absence of pain (AP). In addition, samples were obtained from 15 age-matched healthy controls. Plasma levels of soluble ICAM-1 and ELAM-1 were measured by sensitive ELISA assays.

*Results:*

| | Angina pts | | Pts with NCCP | | Controls |
|---|---|---|---|---|---|
| | DP | AP | DP | AP | |
| sICAM | 338 ± 37* | 272 ± 33 | 239 ± 22 | 231 ± 29 | 220 ± 18 |
| sELAM | 46.1 ± 4.7 | 44.3 ± 5.1 | 46.1 ± 7.8 | 48.3 ± 6.0 | 43.6 ± 3.7 |

Mean ± SEM, ng/ml; *$p < 0.05$ vs. controls.

*Conclusion:* During angina episodes a selective increase in plasma level of the soluble adhesion molecule ICAM-1 was noted, possibly reflecting endothelial cell activation during myocardial ischemia.

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## 780-6 Is elevated plasma histamine levels in the coronary venous blood associated with disease activity in variant angina?

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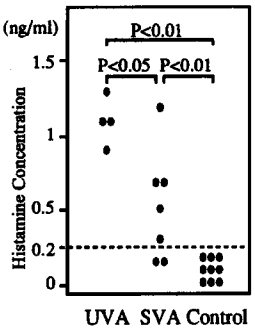
It has been debated whether plasma histamine, a potent vasoconstrictor, is associated with the pathogenesis of variant angina. We measured plasma histamine concentration (PHC) in the great cardiac vein (GCV) in 19 patients; 4 patients with unstable variant angina (UVA) defined as new or worsening angina at rest, 7 patients with stable variant angina (SVA) whose anginal attacks were well controled by drug therapy, and 8 control patients. Intracoronary administration of acetylcholine provoked significant vasospasm in the proximal lesion of the left anterior descending coronary in all patients with UVA and SVA. Blood was sampled from the 5 Fr. NIH catheter positioned at GCV every four hours over a night in all patients. We detected elevation of PHC in all UVA (100%, $P < 0.01$ vs control), 5 of 7 SVA (71%, $P < 0.01$ vs. control) and none of control patients. Similarly, PHC elevation was observed in 14 of 18 UVA (78%, $P < 0.001$ vs. SVA and control), 12 of 30 SVA (40%, $P < 0.001$ vs. control) and none of control sampling points. During all the procedures, spontaneous anginal attacks were documented in 3 patients, which occurred at their maximal values of PHC.




Thus, our results showed that elevation of PHC in the coronary venous blood was commonly observed in patients with variant angina, which was associated with disease activity. Conclusively, the present study presented clinical evidence that histamine may well be related to episodes of variant angina as suggested in animal studies.

# 781 Unstable Angina: Interventional Approaches

Wednesday, March 19, 1997, 10:30 a.m.–Noon
Anaheim Hilton and Towers, Pacific C

10:30

## 781-1 Direct Angioplasty May Be Less Advantageous in Patients Presenting Early After Symptom Onset: Results From GUSTO IIb

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In order to evaluate the relationship between time from symptom onset and the benefit of direct angioplasty, we examined the outcomes of 30-day death and the primary endpoint of death, reinfarction, or disabling stroke in the GUSTO IIb direct PTCA substudy according to time to randomization. 1099 patients with available time data were enrolled within 12 hours of symptom onset with ST elevation from 57 centers in 9 countries, and were randomized to either accelerated dose t-PA or direct angioplasty.

| Time to randomization | PTCA (n = 543) | t-PA (n = 556) | Odds Ratio (95% CI) |
|---|---|---|---|
| 0–4 hours (n = 824) | | | |
| Death | 6.0% | 5.9% | 1.01 (0.57, 1.81) |
| Death, reMI, stroke | 10.0% | 12.1% | 0.81 (0.52, 1.25) |
| >4 hours (n = 275) | | | |
| Death | 5.6% | 11.3% | 0.47 (0.19, 1.15) |
| Death, reMI, stroke | 9.9% | 18.8% | 0.47 (0.23, 0.95) |

When time to enrollment was examined as a continuous variable, there was no statistically significant difference in treatment effect of direct angio-